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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,395	GRUBER ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,13,18,57,61,87,88,103,112,130,149,158-186,190 and 192-206* is/are pending in the application.

4a) Of the above claim(s) *103,130 and 149* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13,18,57,61,87,88,112,158-186,190 and 192-206* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on October 8, 2008 is acknowledged and has been entered. Claims 1, 87-88, 176, 190 have been amended. Claims 2-12, 14-17, 19-56, 58-60, 62-86, 89-102, 104-111, 113-129, 131-148, 150-157, 187-189, 191 have been canceled. Claims 1, 13, 18, 57, 61, 87-88, 112, 158-186, 190, 192-206 are pending. Claims 103, 130, 149 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1, 13, 18, 57, 61, 87-88, 112, 158-186, 190, 192-206 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

New Grounds of rejection

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 13, 18, 57, 61, 87-88, 112, 158-186, 190, 192-206 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 57, 87-88 are amended to incorporate the limitation 'sorting by' or 'sorting and' in each of these independent claims. In claim 1 and 57, the amendment states 'sorting by selecting at least two of the probes'. In claim 87, the amendment states 'configuring an array of at least two probes by sorting and selecting each probe'. In claim 88, the amendment states 'sorting and selecting at least two of the probes for inclusion in the array'. The specification does not include any mention of the terms 'sort' or 'sorting.' While the specification teaches selecting probes for inclusion in the array, as claimed, there is no indication of sorting of the probes or traps. Applicant has not pointed to specific or general support for the amendment. Therefore, because these amendments to the independent claims are not properly supported, the newly added limitations represent new matter in the claims, in both the independent and dependent claims.

Claim Interpretation

The term "wherein the probes which react with the targets are segregated from the remaining probes" is not explicitly defined in the specification. Therefore, the term is being broadly interpreted as reading on the claimed optional lack of interaction with the target and therefore no segregation is performed. In this case a 102 over Grier (6,416,190) will be applied. Stated more plainly, claim 57 requires introducing a target and "determining the reaction or lack thereof, of each of the trapped probes with each of the targets, wherein the probes which react

with the targets are segregated from the remaining probes." Therefore, the claim encompasses embodiments where a target is introduced and no reaction occurs and therefore no segregation would be necessary. In a more narrow interpretation where targets are reacted and interact, segregation, by movement is viewed as obvious in view of the independent movement taught by Grier (6,055,106). In this case, a 103 over Grier in view of Ulmer and Visscher will be applied.

Previous Grounds of Rejection

Claim Rejections - 35 USC § 102

1. Claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184, and 192-206 are rejected under 35 U.S.C. 102(e) as being anticipated by Grier II (US Patent 6,416,190; July 2002). Grier II teaches an apparatus and method for manipulating particles using optical traps (Abstract).

With regard to claim 1, Grier teaches a method of configuring and tracking an array of probes comprising:

a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);

b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array);

c) sorting by selecting at least two of the probes for inclusion in an array of probes contained within the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics); and,

e) tracking the position of at least one of the trapped probes in the array by computerized monitoring of the position of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles through monitoring of their position).

With regard to claim 13, Grier teaches an embodiment of claim 1, wherein the trapped probe is a chemical compound or biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 18, Grier teaches an embodiment of claim 1 wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA or combinations thereof (col. 2, lines 44-48, where the

material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 57, Grier teaches a method of assaying biological material comprising:

a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);

b) providing a fluid media in the vessel; providing at least two probes for biological materials within the fluid media (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array);

c) sorting by selecting at least two of the probes for inclusion in an array based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

introducing into the vessel at least one target comprised of a biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed); and, determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are segregated from the remaining probes (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed).

With regard to claim 61, Grier teaches an embodiment of claim 57, wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA at combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 87, Grier teaches a method of configuring an array of probes comprising:

a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);

b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array); and,

c) configuring an array of at least two probes by sorting and selecting each probe with a corresponding one of the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

wherein said array is modifiable by removing or adding at least one probe in said array (col. 7, lines 44-50, where the optical traps can be used to 'remove or add particles at various optical trap sites').

With regard to claim 88, Grier teaches a method of configuring and reconfiguring an array of probes comprising:

a) directing a focused beam of light at a phase patterning optical element to form a plurality of beamlets emanating from the phase patterning optical element (col. 4, lines 52-65);

b) directing the plurality of beamlets at the back aperture of a focusing lens to pass the beamlets through the focusing lens and converge the beamlets emanating from the focusing lens to generate independently movable optical traps within a vessel (col. 5, lines 22-30, where a focusing optical element converges the beams);

c) providing a plurality of probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are a plurality of probes or particles trapped in the array);

d) sorting and selecting at least two of the probes for inclusion in the array of probes contained within the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

e) trapping each of the selected probes with said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics); and,

f) altering the position of at least one of the probes contained within the array by moving the optical trap containing the probe to reconfigure the array of probes contained within the optical traps (col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 112, Grier teaches an embodiment of claim 1, wherein the movement of the trapped probes are tracked based on pre-determined movement of each optical

trap caused by encoding the phase patterning optical element (col. 7, line 63 to col. 8, line 12, where the hologram is computer designed and provides a pattern of phase modulations).

With regard to claim 159, Grier teaches an embodiment of claim 57, wherein the trapped probe is comprised of one of a biological material or a chemical compound (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed).

With regard to claim 162, Grier teaches an embodiment of claim 57, wherein each optical trap is movable independently (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 163, Grier teaches an embodiment of claim 57, wherein the movement of each optical trap is controlled by a computer (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram, which is controlled by a computer).

With regard to claim 166 and 170, Grier teaches an embodiment of claim 165 and 169, further comprising using the computer to direct the movement of one or more optical traps based on the analysis of the optical data stream (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram, which is controlled by a computer).

With regard to claim 175 and 206, Grier teaches an embodiment of claim 57, wherein the optical traps are formed of two or more of optical tweezers, optical vortices, optical bottles, optical rotators, and light cages (col. 8, lines 11-12, where the optical traps are optical tweezers).

With regard to claim 176, Grier teaches an embodiment of claim 57, wherein at least two of the probes have binding or reactivity characteristics that differ from one another and at least one of the probes is sorted and selected by segregating the probe based on its different binding or reactivity characteristic by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics; and col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 181, Grier teaches an embodiment of claim 176, wherein the predetermined location is one of a physical sub-cell or an optical sub-cell (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics; and col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 184, Grier teaches an embodiment of claim 57, wherein the probes are all directly trapped by the optical trap (col. 8, lines 11-12, where the optical traps are optical tweezers and where these probes or particles are directly trapped).

With regard to claim 194, Grier teaches an embodiment of claim 193, wherein the phase patterning optical element has a static surface having two or more discrete regions and the position of at least one optical trap is altered by changing the discrete region of the static surface

to which the beam of light is directed (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 201, Grier teaches an embodiment of claim 200, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element alters the position of the at least one optical trap (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 192 and 205, Grier teaches an embodiment of claim 88 or 176, wherein the probes are segregated using movement by optical traps, flow channels or micro-capillaries (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 193, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a static surface (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element).

With regard to claim 194, Grier teaches an embodiment of claim 193, wherein the static surface is comprised of two or more discrete regions (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 195, Grier teaches an embodiment of claim 194, wherein the position of at least one of the probes contained within the optical traps is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 4, lines 52-65; col.

5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 196, Grier teaches an embodiment of claim 195, wherein the static surface is substantially continuously varying (Figure 5, where continuous translation of the optical traps are possible; see col. 5, lines 61-67).

With regard to claim 197, Grier teaches an embodiment of claim 194, wherein the position of the at least one optical trap is altered by changing the region of the static surface to which the beam of light is directed (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 198, Grier teaches an embodiment of claim 88, wherein the beam altering optical element is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 199, Grier teaches an embodiment of claim 194, wherein each discrete region is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 200, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element is dynamic (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram and where this can be dynamically altered).

With regard to claim 202, Grier teaches an embodiment of claim 200, wherein the form of at least one of the optical traps is changed by varying the dynamic phase patterning optical

element (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 203, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a discrete static surface, and wherein a form of at least one of the optical traps is changed by moving the discrete static surface (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 204, Grier teaches an embodiment of claim 202, wherein the varying of the dynamic phase patterning optical element is a change in a hologram encoded on its surface (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 177-180, 182-183 and 185-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier II (US Patent 6,416,190; July 2002) as applied to claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184 and 192-206 above, and further in view of Shivashankar et al. (US Patent 6,139,831; October 2000). Grier II teaches an apparatus and method for manipulating particles using optical traps (Abstract).

Grier teaches all of the limitations of claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184 and 192-206 as recited above. Grier does not teach that the probes are bound to a substrate. Shivashankar teaches the use of optical traps in connection to substrate arrays (Abstract).

With regard to claim 177, Shivashankar teaches an embodiment of claim 176, wherein at least one of the probes is one of bound to a substrate or unbound to a substrate (Figure 5B, where particles trapped in an optical tweezer are grafted onto a substrate).

With regard to claim 178, Shivashankar teaches an embodiment of claim 177, wherein all the substrate bound probes having the same binding or reactivity characteristic are labeled with the same markers (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 179, Shivashankar teaches an embodiment of claim 178, wherein at least one of the markers is a wavelength specific dye (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 180, Shivashankar teaches an embodiment of claim 179, wherein at least one of the substrate bound probes is selected by measuring the spectral response of the wavelength specific dye and using the spectral measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C)

With regard to claim 182, Shivashankar teaches an embodiment of claim 177, wherein at least one of the probes is bound to a substrate labeled with a wavelength specific marker and the at least one bound probe is selected by spectroscopically measuring the marker and using the

spectroscopic measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 183 and 186, Shivashankar teaches an embodiment of claim 57, further comprising moving at least one of the trapped probes by transferring the probe from one optical trap to another (coll. 18, lines 9-30).

With regard to claim 185, Shivashankar teaches an embodiment of claim 57, wherein at least some probes are bound to a substrate and at least some probes are unbound to substrate (Figure 5B, wher particles trapped in an optical tweezer are grafted onto a substrate).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success. As taught by Shivashankar, "by using an optical tweezer as a non-invasive tool, a particle coated with a molecule, such as a biomolecule, can be selected and grafted onto spatially localized positions of a semiconductor substrate" (col. 18, lines 31-41). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success.

3. Claims 1, 13-18, 57, 61, 87-88, 112 and 158-176, 181, 184, 190 and 192-206 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier I (US Patent 6,055,106; April 2000) in view of Ulmer et al. (US Patent 5,776,674; July 1998) and further in view of Visscher et al.

(IEEE Journal of Selected Topics in Quantum Electronics, 1996, vol. 2, p. 1066-1076). Grier teaches an apparatus and method for manipulating particles using optical traps (Abstract).

With regard to claim 1, Grier teaches a method of configuring and tracking an array of probes comprising:

a) generating at least two independently movable optical traps within a vessel (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);

b) providing at least two probes within the vessel (col. 2, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 2, lines 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry applications and manipulation of biological materials);

c) sorting by selecting at least two of the probes for inclusion in an array of probes contained within the optical traps (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 2, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);

d) trapping each of the selected probes with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers); and,

e) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 13, Grier teaches an embodiment of claim 1, wherein the trapped probe is one of a chemical compound or a biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 18, Grier teaches an embodiment of claim 1 wherein the trapped probe is an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA or combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 57, Grier teaches a method of assaying biological material comprising:

a) generating at least two independently movable optical traps within a vessel (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);

b) providing a fluid media in the vessel; providing at least two probes for biological materials within the fluid media (col. 2, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 2, lines 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry

applications and manipulation of biological materials);

c) sorting by selecting at least two of the probes for inclusion in an array based on predetermined binding and reactivity characteristics of the probes (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 2, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);

d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers);

e) introducing into the vessel at least one target comprised of a biological material (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 61, Grier teaches an embodiment of claim 57, wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA at combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 87, Grier teaches a method of configuring an array of probes comprising:

a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);

b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array); and,

c) configuring an array of at least two probes by sorting and selecting each probe with a corresponding one of the optical traps (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);

wherein said array is modifiable by removing or adding at least one probe in said array (col. 7, lines 44-50, where the optical traps can be used to 'remove or add particles at various optical trap sites');

d) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 88, Grier teaches a method of configuring and reconfiguring an array of probes comprising:

a) directing a focused beam of light at a phase patterning optical element to form a plurality of beamlets emanating from the phase patterning optical element (col. 4, lines 29-65, specifically lines 29-42, where light passes through a diffractive optical element and a plurality of beams are created);

b) directing the plurality of beamlets at the back aperture of a focusing lens to pass the beamlets through the focusing lens and converge the beamlets emanating from the focusing lens to generate independently movable optical traps within a vessel (col. 3, lines 36-40, where one or

more beams of light are projected into the center of a back aperture; col. 4, line 66 to col. 5, line 7);

c) providing a plurality of probes within the vessel (col. 1, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 1, lnes 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry applications and manipulation of biological materials);

d) sorting and selecting at least two of the probes for inclusion in the array of probes contained within the optical traps (col. 1, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 1, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);

e) trapping each of the selected probes with said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers); and,

f) altering the position of at least one of the probes contained within the array by moving the optical trap containing the probe to reconfigure the array of probes contained within the optical traps (col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);

g) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 112, Grier teaches an embodiment of claim 1, wherein the movement of the trapped probes are tracked based on pre-determined movement of each optical trap caused by encoding the phase patterning optical element (col. 2, lines 41-45, where an object of the invention is to create multiple independently steered optical traps; col. 5, lines 38-52).

With regard to claim 159, Grier teaches an embodiment of claim 57, wherein the trapped probe is comprised of one of a biological material or a chemical compound (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 161, Grier teaches an embodiment of claim 57, further comprising altering a position of at least one trapped probe in the array by moving the optical trap containing the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 162, Grier teaches an embodiment of claim 57, wherein each optical trap is movable independently (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 163, Grier teaches an embodiment of claim 57, wherein the movement of each optical trap is controlled by a computer (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 164, Grier teaches an embodiment of claim 160, further comprising receiving the optical data-stream with a computer (Figure 10, where a personal computer is included for imaging of the particles).

With regard to claim 166 and 170, Grier teaches an embodiment of claim 165 and 169, further comprising using the computer to direct the movement of one or more optical traps based on the analysis of the optical data stream (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 175 and 206, Grier teaches an embodiment of claim 57 and 88, wherein the optical traps are formed of two or more of optical tweezers, optical vortices, optical bottles, optical rotators, and light cages (col. 5, lines 12-21, where the optical traps are optical tweezers).

With regard to claim 176, Grier teaches an embodiment of claim 57, wherein at least one of the probes is selected by segregating the probe by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 181, Grier teaches an embodiment of claim 176, wherein the predetermined location is one of a physical sub-cell or an optical sub-cell (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 184, Grier teaches an embodiment of claim 57, wherein the probes are all directly trapped by the optical trap (col. 6, lines 9-12, where the probes are stably trapped in the optical trap).

With regard to claim 194, Grier teaches an embodiment of claim 193, wherein the phase patterning optical element has a static surface having two or more discrete regions and the position of at least one optical trap is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 201, Grier teaches an embodiment of claim 200, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element alters the position of the at least one optical trap (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another).

With regard to claim 192 and 205, Grier teaches an embodiment of claim 88 and 176, wherein the probes are segregated using movement by optical traps, flow channels or micro-capillaries (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 193, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a static surface (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 195, Grier teaches an embodiment of claim 194, wherein the position of at least one of the probes contained within the optical traps is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 196, Grier teaches an embodiment of claim 195, wherein the static surface is substantially continuously varying (col. 5, lines 22-36, where in this embodiment a system is constructed that carries out continuous translation of the optical tweezer trap).

With regard to claim 197, Grier teaches an embodiment of claim 194, wherein the position of the at least one optical trap is altered by changing the region of the static surface to which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 198, Grier teaches an embodiment of claim 88, wherein the beam altering optical element is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 199, Grier teaches an embodiment of claim 194, wherein each discrete region is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 200, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element is dynamic (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 202, Grier teaches an embodiment of claim 200, wherein the form of at least one of the optical traps is changed by varying the dynamic phase patterning optical

element (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 203, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a discrete static surface, and wherein a form of at least one of the optical traps is changed by moving the discrete static surface (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 204, Grier teaches an embodiment of claim 202, wherein the varying of the dynamic phase patterning optical element is a change in a hologram encoded on its surface (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram; col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

Regarding claims 1, 57 and 87-88, Grier does not teach the limitation of selecting probes based on predetermined binding and reactivity characteristics of the probes or probes that have predetermined binding and reactivity characteristics. Regarding claim 57, Grier does not teach the step of determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are segregated from the remaining probes. Regarding claim 176, Grier does not teach the segregation of probes based on binding reactivity.

With regard to claims 1, 57 and 87-88, Ulmer teaches sorting and selecting probes based on predetermined binding and reactivity characteristics of the probes and that the probes have

predetermined binding and reactivity characteristics (col. 7, lines 28-35, where the trapped probe is an oligonucleotide or nucleic acid fragment)

With regard to claim 57, Ulmer teaches an embodiment comprising determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are sorted and segregated from the remaining probes (col. 7, lines 16-44, where probes that are bound to the target are separated from the remaining probes).

With regard to claim 176, Ulmer teaches an embodiment of claim 57, wherein at least two of the probes have binding or reactivity characteristics that differ from one another and at least one of the probes is sorted and selected by segregating the probe based on its different binding or reactivity characteristic by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, lines 16-44, where probes that are bound to the target are separated from the remaining probes).

Regarding claims 1 and 87-88, while Grier teaches the use of a personal computer to identify particles, Grier does not explicitly teach computerized monitoring of the positions of the optical traps. Visccher teaches an overview of the construction of multiple-beam optical traps and includes different methods of monitoring (Abstract).

With regard to claim 1, Visccher teaches tracking a position of at least one optical trap by computerized monitoring (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claims 87-88, Visccher teaches tracking a position of at least one of the trapped probes in the array by computerized monitoring of the position of the optical trap which

contains it (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 158, Visccher teaches an embodiment of claim 57, further comprising tracking the position of at least one of the trapped probes by monitoring the position of the optical trap which contains it (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 160, Visccher teaches an embodiment of claim 57, further comprising producing an optical data stream of data corresponding to the identity and position of at least one of the optical traps (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 164, Visccher teaches an embodiment of claim 160, further comprising receiving the optical data-stream with a computer (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system).

With regard to claim 165, Visccher teaches an embodiment of claim 164, further comprising analyzing the optical data stream with the computer (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope and includes subsequent analysis).

With regard to claim 167-169, Visccher teaches an embodiment of claim 166, further comprising converting the optical data-stream to a video signal, receiving the video signal and analyzing the video signal with a computer (p. 1070-1073, where position detection options are

discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system).

With regard to claim 171, Visccher teaches an embodiment of claim 170, wherein the video signal is used to produce an image (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system; Figure 7, where an image is produced).

With regard to claim 172, Visccher teaches an embodiment of claim 171, further comprising viewing the image and directing the movement of one or more of the optical traps based on the viewing of the image (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system; Figure 7, where an image is produced).

With regard to claim 173, Visscher teaches an embodiment of claim 160, wherein the data is spectroscopic data (p. 1070-1073, where position detection options are discussed and include a variety of position detection data types).

With regard to claim 174, Visscher teaches an embodiment of claim 173, further comprising using a computer to direct the movement of one or more optical traps based on an analysis of the spectroscopic data (p. 1070-1073, where position detection options are discussed; see also p. 1074, where the position detection is carefully calibrated).

With regard to claim 190, Visscher teaches an embodiment of claim 57, wherein the movement of at least one optical trap is selected from one or more of the group consisting of rotation in a fixed position, rotation in a non- fixed position, movement in two dimension, and movement in three dimensions (p. 1070-1076, where a variety of types of movement are detected in different dimensions, depending on the format of position detection chosen).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the probe with predetermined binding and reactivity characteristics as taught by Ulmer into the method of optical trapping taught by Grier to arrive at the claimed invention with a reasonable expectation for success. Ulmer discloses the use of optical traps in methods of biological, biochemical or chemical processes. As taught by Ulmer, "Examples of chemical, biochemical and/or biological processes that might be implemented in accordance with the invention include the following: oligonucleotide synthesis and sequencing, carbohydrate synthesis and sequencing, combinatorial library synthesis and screening, conventional (i.e., Sanger or Maxam-Gilbert) DNA sequencing, or single-molecule DNA sequencing" (Abstract). Specifically regarding binding and reactivity characteristics of the probes, Ulmer teaches, "procedures which permit the identification and isolation of the desired DNA fragment from among the background of undesired DNA fragments. The optical trap described herein may be used to simplify or obviate these latter procedures". Ulmer also teaches, "a probe (a nucleic acid fragment that specifically binds to the desired nucleic acid fragment) is necessary. The probe is coupled to a particle suitable for trapping in the optical trap. One or more of the particle-coupled probes are then applied to thin film 110 in a first droplet 112. The optical trap is then used to select one of the particle-coupled probes in its optical beam

and move the particle-coupled probe through thin film 110 (col. 7, lines 28-35)." In fact, it is also a directly stated object of Grier to "provide an improved method and system for establishing a plurality of optical traps for a variety of commercial applications relating to manipulation of small particles" and this includes chemical and biochemical sensor arrays, facilitation of combinatorial chemistry applications and the manipulation of biological materials (col. 1, lines 48-57). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the arrays of optical traps taught by Grier to include the specific types of biological targets and probes with predetermined or predefined binding and reactivity characteristics as taught by Ulmer to achieve the manipulation of biological targets as described generally by Grier with a reasonable expectation for success.

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Grier and Ulmer to incorporate the computerized monitoring of Visscher to arrive at the claimed invention with a reasonable expectation for success. As taught by Visccher, "sensitive position detectors for objects trapped by the system are required. A wide temporal bandwith is desirable for such detectors (>10 kHz), especially for calibration of optical trap stiffness)" (p. 1066, col. 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Grier and Ulmer to incorporate the computerized monitoring of Visscher to arrive at the claimed invention with a reasonable expectation for success.

4. Claims 177-180, 182-183 and 185-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier I (US Patent 6,055,106; April 2000) in view of Ulmer et al. (US Patent

5,776,674; July 1998) and further in view of Visscher et al. (IEEE Journal of Selected Topics in Quantum Electronics, 1996, vol. 2, p. 1066-1076) as applied to claims 1, 13, 18, 57, 61, 87-88, 112 and 158-176, 181, 184, 190, 192-206 above and further in view of Shivashankar et al. (US Patent 6,139,831; October 2000). Grier I teaches an apparatus and method for manipulating particles using optical traps (Abstract).

Grier I teaches all of the limitations of claims 1, 13, 18, 57, 61, 87-88, 112 and 158-164, 166-176, 181, 184, 190 and 192-206 as recited above. Grier does not teach that the probes are bound to a substrate. Shivashankar teaches the use of optical traps in connection to substrate arrays (Abstract).

With regard to claim 177, Shivashankar teaches an embodiment of claim 176, wherein at least one of the probes is one of bound to a substrate or unbound to a substrate (Figure 5B, wher particles trapped in an optical tweezer are grafted onto a substrate).

With regard to claim 178, Shivashankar teaches an embodiment of claim 177, wherein all the substrate bound probes having the same binding or reactivity characteristic are labeled with the same markers (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 179, Shivashankar teaches an embodiment of claim 178, wherein at least one of the markers is a wavelength specific dye (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 180, Shivashankar teaches an embodiment of claim 179, wherein at least one of the substrate bound probes is selected by measuring the spectral response of the wavelength specific dye and using the spectral measurement to select the at least one probe (col.

17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C)

With regard to claim 182, Shivashankar teaches an embodiment of claim 177, wherein at least one of the probes is bound to a substrate labeled with a wavelength specific marker and the at least one bound probe is selected by spectroscopically measuring the marker and using the spectroscopic measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 183 and 186, Shivashankar teaches an embodiment of claim 57, further comprising moving at least one of the trapped probes by transferring the probe from one optical trap to another (coll. 18, lines 9-30).

With regard to claim 185, Shivashankar teaches an embodiment of claim 57, wherein at least some probes are bound to a substrate and at least some probes are unbound to substrate (Figure 5B, where particles trapped in an optical tweezer are grafted onto a substrate).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success. As taught by Shivashankar, "by using an optical tweezer as a non-invasive tool, a particle coated with a molecule, such as a biomolecule, can be selected and grafted onto spatially localized positions of a semiconductor substrate" (col. 18, lines 31-41). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments filed October 8, 2008 have been fully considered but they are not persuasive.

First, it is noted that the main points discussed with Applicant's representative were not fully addressed in the instant response. Hopefully, the response to Applicant's arguments helps clarifies where differences remain between Applicant's argued position, the instantly claimed invention and the prior art as interpreted by the Examiner. Specifically, Applicant noted in the interview that the instant claims are directed to a spatial light modulator and that certain features distinguish over the prior art of record, particularly as relates to 3D trapping versus 2D trapping. Applicant's arguments were carefully reviewed, but other than in reference to Ulmer, it does not appear that this distinction was addressed. Next, the issues of the selection process and the inherency of the binding properties of the probes were discussed, but were not addressed in detail. Further, the issue of sorting raised an issue of new matter in the instant specification. Finally, regarding Shivashankar, Applicant's representative indicated in interview that the features of the optical trapping between Shivashankar and Grier were incompatible with one another. However, again, these differences were not addressed in detail. Therefore, for these reasons and the reasons stated in more detail below, Applicant's arguments were not persuasive.

First, Applicant traverses the rejection of claims 1, 57, 87-88 as being anticipated by Grier '190 (Grier II in the instant rejection). Applicant asserts that Grier does not teach the elements of the instantly claimed invention. Applicant states "Grier '190 discloses a method and

apparatus of using optical tweezers to control optical trap arrays in three dimensions, using computer generated holograms" and "includes an adaptive tweezer mode where a movable knife edge is moved into the path of several laser beams". Applicant also states "Grier '190 does not teach or suggest sorting or selecting at least two probes for inclusion in the array" and "there is no segregation of particles which react with targets, disclosed or taught by Grier '190". Applicant also argues "the Examiner misunderstands the adaptive tweezer mode and the movable knife edge in Grier '190. The knife edge simply blocks beams of light from forming optical traps, such that optical traps are formed in a controlled way, and the particles fill the optical traps in a predetermined format. This is not related to computerized tracking of the optical traps" (p. 17 of remarks). Regarding claims 163-164, 166 and 170, Applicant asserts "the Examiner has misunderstood controlling of the diffractive optical element using a computer, to produce holograms, in Grier '190, with the control of the optical traps by a computer 38 (see Fig. 3B), where the optical data stream 32 (including a video signal) is monitored and analyzed in order to control movement of the optical traps" (p. 18 of remarks). Regarding claims 176, 181, 192, 206, Applicant argues "the particles in Grier '190 are not sorted and selected by segregating them based on their different binding or reactivity characteristics, nor by moving the particles to a predetermined location in a vessel" (p. 19 of remarks). Regarding claims 194-197, Applicant argues that "Grier '190 does not teach or suggest a method of configuring or reconfiguring an array of probes wherein the static surface is comprised of two or more discrete regions, as recited in claim 194". Applicant also states "although Grier '190 disclose a diffractive optical element with a static surface, the ability to move the discrete static surface, or have two or more discrete regions in the static surface, and these discrete regions being able to be changed, and thus,

altering the position of the probes or the optical traps, thereby are not taught or suggested by Grier '190" (p. 19 of remarks).

These arguments have been carefully considered, but are not persuasive. First, it is noted that the specification does not teach sorting of probes within the array and therefore the meaning of the term is unclear and is therefore considered as addressed with the previous rejection of the claims. However, it is also noted that Grier '190 teaches sorting of the traps according to size, for example (see col. 7, line 61-62). While Applicant is correct that segregation does not explicitly occur, it is noted in response that the claim is being interpreted broadly, as noted in the claim interpretation stated above, the term "is not explicitly defined in the specification. Therefore, the term is being broadly interpreted as reading on the claimed optional lack of interaction with the target and therefore no segregation is performed". Stated more plainly, claim 57 requires introducing a target and "determining the reaction or lack thereof, of each of the trapped probes with each of the targets, wherein the probes which react with the targets are segregated from the remaining probes." Therefore, the claim encompasses embodiments where a target is introduced and no reaction occurs and therefore no segregation would be necessary. In this interpretation of the claim, Grier 190 anticipates the claim.

Furthermore, Figure 9 clearly shows a variety of optical traps in an array format, that the traps can be added or removed from within the array and that they can be independently moved or manipulated and the presence of multiple optical traps within the array (col. 7, lines 44-60). Grier teaches that these traps can comprise biological elements including a variety of cell types (see Examples 1-3) or chloroplasts (col. 12, lines 31-34), and that these traps are which meets the limitation of the claim. It is also noted again that the "predetermined binding and reactivity

characteristics" of a biological sample, including a cell, a chloroplast or genetic material, represent an inherent characteristic that present in that individual biological sample or samples. Applicant's arguments regarding the movable knife edge and the role of filling the traps is also noted. However, these arguments do not clarify the invention of Grier in comparison to the instant invention. As noted above, particularly with regard to claim 1, Grier 190 teaches the elements of the claim as stated in the rejection above. Without a clear explanation of how a movable knife edge for control of loading of a trap does not meet the limitation as claimed, the arguments are not persuasive. Furthermore, regarding Applicant's arguments that the knife edge "is not related to computerized tracking" and that Grier 190 does not teach computerized monitoring of the trapped probes, it is unclear how the statement in the specification as noted in the rejection above, that "one can also image an array of the particles **126** in the manner shown in FIG. 10. A microscope **138** can image the particles **126**, and a personal computer **140** can identify the particles **126**" (col. 7, line 63) does not meet the limitation of computerized monitoring of an optical trap. Clarification of this issue is requested. These same arguments above apply in response to the arguments over the dependent claims, as well. The rejections are maintained.

Applicant traverses the rejection of claims 177-180, 182-183 and 185-186 over Grier '190 in view of Shivashankar, Applicant argues "Shivashankar disclose an apparatus and method for immobilizing molecules on a substrate" and the coating on the substrate "is impinged with a laser beam to form patterns of melting and ablation on the substrate to which insoluble particles are adhered and immobilized". Applicant also argues "although in one embodiment an optical

tweezers is used, it is used simply to emit the laser beam such that the beam impinges on the substrate, heats it, and then the optical tweezer can move the selected particle to the area of impingement to immobilize the particle" (p. 28 of remarks). Applicant argues that Shivashankar does not teach probes having the same binding or reactivity characteristics are labeled with the same marker, that probes are selected, or that probes are transferred from one trap to another (p. 28 of remarks). Applicant also argues "Shivashankar... only discloses that a molecule coated particle can be exposed to a fluorescently labeled complementary sequence for detection" and that "using spectroscopical measurement of the marker to select a particular probe, is not taught or suggested by Shivashankar et al." (p. 28 of remarks).

These arguments have been considered but are not persuasive. First, it is noted that Shivashankar is relied upon for teaching binding of wavelength specific dyes to individual probes, elements that are taught by Shivashankar. Binding of complementary sequences is an example where probes with the same reactivity characteristic (in this case, sequence) would necessarily bind to the same marker, which would aid in future selection of the probes to which the sequence was bound. Furthermore, the passage of col. 18, lines 9-30 teaches that multiple (or n) particles with unique DNA sequences attached are transferred into individual optical traps and then transferred and grafted onto the substrate. Therefore, Applicant's arguments are not persuasive and the rejection is maintained.

Applicant traverses the rejection of claims 1, 57, 87 and 88 as being obvious over Grier '106 (Grier I in the instant rejection) in view of Ulmer and Visscher. Applicant again argues "Grier '106 precedes '190, and thus, is directed simply to creating holographic optical traps." and

states "Grier '106 fails to disclose any method of sorting and selection of the type of particles based on any predetermined characteristics of those particles" and "do not disclose computerized tracking of any preselected particles" (p. 21 of remarks). Regarding Ulmer, Applicant argues "Ulmer discloses only trapping one particle-coupled probe which is then moved from a first droplet 112, through the thin film 110 into the second droplet 114 – in two dimensions. There is no array formed" and then, the "resulting complex is then moved by the optical trap through thin film 110 to another droplet 116, where it is collected and manipulated" (p. 21 of remarks). Applicant attempts to distinguish Ulmer over the instant claims by stating "multiple traps are created, which are independently movable in a vessel-i.e., in three dimensions, not two dimensions, as in Ulmer" And "since there is no array formed, there are no tracking, or sorting functions performed" and that "the computer 400 used in Ulmer is not for monitoring the position of the optical trap which contains the probe – rather, it is for storing information on the fluorescent photon events, and identifying the nucleotides" (p. 22 of remarks). Further regarding Grier '106, Applicant argues "the Examiner has misunderstood controlling the diffractive optical element using a computer to produce a holograms, in Grier 106, with the control of optical traps by a computer 38 (see Fig. 3B), where the optical data stream 32 (including video signal) is monitored and analyzed in order to control movement of the optical traps. Finally, Applicant notes "Grier '106 is silent with respect to any computer control of the optical traps or of analyzing an optical data stream, where data is spectroscopic data" (p. 25 of remarks). Applicant also notes "although Grier '106… discloses a diffractive optical element with a static surface", Applicant argues that Grier does not teach the ability to move the surface and does not teach that this can be useful in altering the position of probes (p. 27 of remarks).

These arguments have been carefully considered but are not persuasive. First, it is noted that Grier '106 is not relied upon as an anticipation rejection. It was made clear in the art rejection above, while Grier captures biological samples and renders obvious the elements of the optical trapping aspects of the method, Grier is not explicit about binding or reaction between captured biological entities. However, despite Applicant's argument regarding computer control of the optical traps, Grier teaches "The diffractive optical element 40 can include computer generated holograms which split the input light beam 12 into a preselected desired pattern. Combining such holograms with the remainder of the optical elements in FIGS. 3 and 4 enables creation of arbitrary arrays in which the diffractive optical element 40 is used to shape the wavefront of each diffracted beam independently. Therefore, the optical traps 50 can be disposed not only in the focal plane 52 of the objective lens 20, but also out of the focal plane 52 to form a three-dimensional arrangement of the optical traps 50." (col. 4, lines 56-65). Regarding the phase patterning element, Grier teaches, "in the optical tweezer system 10 either static or time dependent diffractive optical elements 40 can be used. For a dynamic, or time dependent version, one can create time changing arrays of the optical traps 50 which can be part of a system utilizing such a feature. In addition, these dynamic optical elements 40 can be used to actively move particles and matrix media relative to one another" (col. 5, lines 12-21). Therefore, Grier renders obvious the elements of the optical trap as claimed, for the reasons stated above.

Ulmer is relied upon for teaching interaction and binding between a captured sequence specific probe and a target and that probes that are bound to a target are separated or segregated away (col. 7, lines 16-44). It is again noted that each of these captured sequences each have reactivity and binding characteristics that are unique and inherent for each sequence or biological

sample. While Applicant is correct that Ulmer teaches capture of oligonucleotides and movement of the captured sequence in two dimensions, the specific circumstances of the capture of these sequences does not interfere with or teach away from extending the general teaching of Grier '106 to "provide a novel method for manipulating a plurality of biological objects" to include analysis, manipulation and or binding between specific biological molecules, including DNA targets and probes. The general teaching of capture of oligonucleotides in optical traps is provided by the general teaching of Ulmer, regardless of the presence of the traps or their movement in one, two or three dimensions. Finally, regarding Visscher, while Applicant's argument that "Visscher et al. disclose that the method is relatively 'insensitive' to the absolute location of a trapped particle within the field of view (see Abstract), that single statement does not provide a clear picture of the overall teaching of Visscher. For example, while Applicant states "Visscher et al. only disclose the stiffness of an optical trap, and any references to multiple traps states that the traps are not independently movable", this statement is also a single passage in a reference which teaches a variety of embodiments useful for position detection using microscopy and computerized monitoring. While Visscher include embodiments directed to stiffness of optical traps, or to embodiments that are relatively insensitive to absolute location, the majority of the reference is directed to position detection. Visscher teaches, for example, "Combining optical tweezers with position detectors enables the development of feedback systems to create either isometric "position" clamps (used to keep the position of the trapped particle constant) or isotonic "force" clamps (used to keep the force on a trapped particle constant)" (p. 1066, col. 1). Visscher also teaches, "videorecording the movement on an optical-memory disc recorder (OMDR)" (p. 1074, col 1) and "Nanometer-scale measurement of the

motion of a silica bead (0.5-umdiameter) produced by a single kinesin molecule moving along a microtubule. Data were recorded at 2 kHz, anti-alias filtered at 1 kHz, and median-filtered with a 13-point kernel (see text)." While Visscher does not spend much time discussing the specifics of the data collection process, instances and passages like those quoted above clearly do not represent manual data collection and therefore represent computerized monitoring of position and tracking of traps. Furthermore, the image processor, Argus 20 (p. 1072, col. 2), represents another computer format useful in the position detection techniques taught by Visscher. Therefore, in view of the combined teaching of Grier, Ulmer and Visscher, the instant claims are rendered obvious. While Applicant's arguments regarding a lack of motivation are noted, these arguments are not persuasive. Grier lays the foundation for trapping and analysis of biological materials in general. Ulmer provides further motivation for analyzing, trapping and reacting sequence specific DNA probes and Visscher provides the basis for positional detection of the movement of particles trapped in an optical trap. Therefore, the combination of references is proper and renders the claims obvious, as claimed, and the rejections are maintained.

Applicant again traverses the rejection of claims over Grier '106 in view of Ulmer, Visscher and Shivashankar. These arguments were presented, in brief, as argued over Grier '190 above. Applicant argues "Shivashankar disclose an apparatus and method for immobilizing molecules on a substrate" and the coating on the substrate "is impinged with a laser beam to form patterns of melting and ablation on the substrate to which insoluble particles are adhered and immobilized". Applicant also argues "although in one embodiment an optical tweezers is used, it is used simply to emit the laser beam such that the beam impinges on the substrate, heats it,

and then the optical tweezer can move the selected particle to the area of impingement to immobilize the particle" (p. 28 of remarks). Applicant argues that Shivashankar does not teach probes having the same binding or reactivity characteristics are labeled with the same marker, that probes are selected, or that probes are transferred from one trap to another (p. 28 of remarks). Applicant also argues "Shivashankar... only discloses that a molecule coated particle can be exposed to a fluorescently labeled complementary sequence for detection" and that "using spectroscopical measurement of the marker to select a particular probe, is not taught or suggested by Shivashankar et al." (p. 28 of remarks).

These arguments have been considered but are not persuasive. First, it is noted that Shivashankar is relied upon for teaching binding of wavelength specific dyes to individual probes, elements that are taught by Shivashankar. Binding of complementary sequences is an example where probes with the same reactivity characteristic (in this case, sequence) would necessarily bind to the same marker, which would aid in future selection of the probes to which the sequence was bound. Furthermore, the passage of col. 18, lines 9-30 teaches that multiple (or n) particles with unique DNA sequences attached are transferred into individual optical traps and then transferred and grafted onto the substrate. Therefore, Applicant's arguments are not persuasive and the rejection is maintained.

Again it is reiterated that Applicant's arguments were carefully considered. If specific limitations or claims were not addressed in detail in the response noted above, they remain obvious in view of the teachings provided in the rejection(s) stated above and the response

carefully applied over the individual references, either alone or in combination, over the independent claims and their dependent claims, respectively.

Conclusion

No claims are allowed. All claims stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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